converting our major software programs for speech generation and adaptive inputs to the SUMEX AIM system in part so that they can be used by Dr. Colby and his group.

2. Mr. Douglas Appelt, a doctoral student at SU-AI was our principal systems programmer last summer. He is currently doing research in the same area as ours with Dr. Gary Hendrix of SRI. We have used his knowledge of your system (via the message sending routines) to assist us in starting our project. Mr. Appelt will be working with us at MSU again this summer (June-Sept.,1977), and he will be using the SUMEX-AIM system.

C) Critique of resource services.

We have found the HELP files to be a lot of help. We are beginning to understand our own needs and your services to the extent that it may be helpful to meet with one of your staff. Dr. Eulenberg will be in California in early June and plans to visit your facility. However, we have found that your system is easy to use and do not feel more distant from you than from other computer installations on our own campus.

III) <u>Follow-on SUMEX grant period (8/78-7/83).</u>

A) Long-range user project goals and plans.

We want to do fundamental research in artificial intelligence in the context of the generation of speech from very minimal amounts of input. This problem seems closely related to the understanding of speech. It seems that the methods of representation of knowledge used for speech or vision understanding can be used in a natural way for fluent generation of speech. Our area seems almost unique in AI in that it is socially desirable (without question). Even relatively primitive systems can improve the quality of life for hundreds of thousands of people.

Major long range goals are:

1) To do research in transposing the vocal tract to another region of the body in which an individual has suitable myoelectric control for the generation of speech.

2) To define a suitable system of semantics and to encode world knowledge in that system that would be useful for the generation of speech fluently.

3) To discover primitive operations on semantics which allow new and appropriate combinations of speech to be generated. (Using other sources of knowledge.)

4) To develop means for individuals who are physically unable to use standard input devices to program and personalize their own speech and environmental control system.

5) To study means of using speech output to aid blind persons both through experiments with simplified text to speech devices and through means of training blind persons to write in cursive and manuscript.

6) To study the educational consequences of communication aid systems for individuals who, because of previous misdiagnoses as mentally impaired, have been excluded for the mainstream education system.

7) To improve the prosodic qualities of generated speech, using its semantic aspects.

8) To design portable speech prostheses which allow maximum use of state of the art knowledge in speech generation.

9) To develop an experimental base for studing how the concepts which are articulated in speech are manipulated by individuals at differing states of mental organization

10) To study the potential for speech generation systems as a means of stimulating autistic children.

11) To develop voice recognition systems which will aid individuals with limited speech to develop their full potential.

(We don't expect to finish all of these by 1983.)

B) Justification for continued use of SUMEX by your project.

1) We need to use many sources of knowledge represented in computers to do our work, similar to many SUMEX users.

2) We know kindred spirits in the AI community for many of our long range goals.

3) We have substantial hardware and software expertise which we are willing to share.

4) We are making a substantial effort in the practical application of such research and would expect to benefit society.

5) This area does not have a traditional means of support for research separate from development which makes your support vital at this time.

6) Our area is very interdisciplinary and the communication aspects of SUMEX-AIM will be increasing valuable to us.

C) Comments and suggestions for future resource goals, etc.

In view of the fact that we are new members of the community, we do not have any special suggestions for new resource goals at this time.

6.4.2 AI IN PSYCHOPHARMACOLOGY

Artificial Intelligence in Psychopharmacology

Jon F. Heiser, M.D.
Dept. of Psychiatry and Human Behavior
University of California at Irvine

I. Summary Research Program

A. Technical Goals

1. We propose to construct a computer based system embodying some of the knowledge of an expert in clinical psychopharmacology. Such a system could greatly assist physicians and students who are not specialists in the chemotherapy of mental disorders in choosing the best psychopharmacological treatment for patients for whom such treatment is indicated. The system could also serve as a teaching source of psychodiagnostic and psychopharmacological knowledge.

2. The specific aims of this project are:

   - To develop a set of MYCIN type rules which are a model of expert clinical teaching, consulting and decision-making for clinical psychopharmacology.

   - To implement this set of rules in the MYCIN system, and

   - To evaluate the performance of the resulting system as a teaching and consulting aid.

3. No system currently available or under development approaches the goals of the project in the field of clinical psychopharmacology.

4. It is anticipated that the research will fall into two distinct phases each of approximately 18 months duration. The first and current phase involves evaluating the relevance of the structure of the MYCIN system for use in clinical psychopharmacology by replacing the current infectious disease diagnosis and therapy rules and parameters with psychopharmacology rules and parameters. The second phase will involve accumulating a large body of rules and entering them into the MYCIN system and evaluating their performance. Toward the end of this phase, the behavior of the system will be compared with the behavior of recognized experts working on the Adult Inpatient Psychiatric Service of the UCI Medical Center. This evaluation will focus on the adequacy of the system for representing the knowledge of a skilled psychopharmacologist rather than an actual system performance in the clinical framework.

B. Medical Relevance and Collaboration

1. Medical Relevance

a. For many years it has been well recognized that potent, effective psychopharmacological agents are frequently used in an unsystematic and irrational manner. The most prescribed medication in the United States today is diazepam (Valium), a minor tranquilizer. The first six most prescribed medications are all psychoactive agents. In California, instances of repetitive use of psychotropic drugs have been reported by 70% of a random sample of adults. About 30% of the sample had used psychotropic drugs in the preceding twelve months. Another study showed that 20% of a medical population was taking psychoactive agents at any given time. These figures do not include alcoholic beverages or non-prescription and illicit drugs with psychoactive properties. Many persons are advised to ingest a daily pharmacologic stew consisting of one or more neuroleptic agents, an antidepressant, an anti-parkinsonian agent, one or more tranquilizers, a hypnotic and possibly a psychostimulant. These regimens are often complicated by non-prescription remedies, alcoholic beverages and illicit drugs. The inevitable drug-drug interactions affect absorption, distribution, binding metabolism and excretion of many drugs.

b. Each year Americans spend over $700,000,000 for psychotropic drugs. In a recent year $150,000,000 was spent on the anti-anxiety agent chlordiazepoxide (Librium). Between 20 and 25 million prescriptions are written each year for diazepam. It is estimated that 170,000,000 prescriptions for psychotropic drugs were written in 1967, and that 202,000,000 prescriptions were written in 1970, more than one for every person in the United States. About 17% of all prescriptions written are for psychoactive drugs. If we include medications in which a psychotropic drug is combined with an antispasmodic vasodialator, or other agent, probably 25% of all prescriptions contain psychotropic drugs. The vast majority of these prescriptions are written by physicians who are not psychiatrists.

c. Many physicians, including psychiatrists, who are practicing today, completed their formal medical training prior to the 1950's when modern psychopharmacological agents first became available. Their training typically includes no instruction in modern clinical psychopharmacology. Even physicians trained since the mid-1950's cannot be expected to keep abreast of the expanding and changing field of psychopharmacology. The principles and practices recommended a few years ago are rapidly becoming obsolete. A recent study showed that the general knowledge of the pharmacology, physiology, and side effects of psychoactive medications was low in both psychiatrists and non-psychiatrists: less than 20% of the physician subjects were able to devise a psychopharmacologically rational dosage schedule for benzodiazepines. Fifty percent of the non-psychiatrist medical staff felt that doses up to one gram per day of a tricyclic antidepressant, more than three times the recommended maximum and a potentially fatal amount, might be prescribed for depressive symptoms.

d. We estimate that there are at least 25 discrete syndromes currently identified in clinical psychiatry, each of which has a unique hierarchy of pharmacological treatment. Each treatment in each section has its own set of potential side effects, adverse reactions and drug-drug, drug-host, drug-age and drug-state of health interaction. In addition, for each therapeutic regimen in each hierarchy, there are several classes of drugs which typically consist of more than one agent or combination of agents which are potentially beneficial and which can be preferentially ranked dependent on several other factors in the clinical situation.

2. Medical Collaboration

1. The principal investigator, Jon F. Heiser, M.D., is a physician who is board certified in psychiatry and in full time teaching, research and University service.

2. Three medical students have participated in this project to date: Clifford Risk, Dana W. Ludwig, and Sue A. Clear. 3. Two resident physicians have participated in this project: Bronco R. Radisavljevic, M.D., and Steven J. Smith, M.D.

4. A Doctor of Pharmacy participates in the research: Pierre J. Menard, Pharm. D.

C. Progress Summary

1. Our initial endeavors to extend a MYCIN-like system to clinical psychopharmacology have been successful. None of the envisioned or predicted problems related to the vagaries of psychiatric terminology and diagnosis have materialized. The system appears to work promptly and accurately to diagnose psychiatric conditions, and in a very rudimentary form, to suggest appropriate pharmacological treatment.

The current system consists of about 20 clinical parameters and about 50 decision rules aimed chiefly at a small number of diagnosed psychiatric conditions.

The following is an example of a sample consultation but realistic case:

Sample Consultation with HEADMED, a Psychopharmacology Advisory System

Patient History

A 37 year old man was brought into the emergency room by his distraught family members. They described how the patient, a well-liked, successful and cheerful but reserved history professor, had become increasingly outspoken, short-tempered, and inattentive to accepted norms of social behavior over the preceding three weeks. An unprovoked argument and physical assault upon a long-time friend motivated the family to seek professional help.

Results of a physical exam and routine laboratory studies were within normal limits. Consultation with the psychiatric service was requested. A first year psychiatric resident re-interviewed the patient and his family, and completed a formal mental status exam prior to obtaining the following consultation from the system.

[Questions are generated by the system and appear in mixed upper and lower case, user responses are in boldface capitals and follow a double asterisk. Added commentary is indented in italics.]

****

```
Special options (type  for help):
** AFB
Hello, Dr. Bowen
Do you wish to run the consultation program
**YES

29-OCT-76 00:47:26

  --------PATIENT-1--------
  1) PATIENT'S NAME        [The consultation begins with a few standard
                            questions.]
  **JOHN DOE
  2) PATIENT'S AGE IN YEARS
  ** 37
  3) SEX:
  ** MALE
  4) IS John Doe ORIENTED
  ** N
                      [Since the patient is disoriented, the system begins to
                       Probe a little deeper.]
  5) IS John DOE DISORIENTED-TO-PERSON
  ** Y
  6) IS John Doe DISORIENTED-TO-PLACE
  ** N
  7) IS John Doe DISORIENTED-TO-TIME
  ** Y
```

```
  8) PLEASE TYPE IN THE ONE WORD WHICH BEST DESCRIBES THE THOUGHT PATTERNS
     OR THOUGHT DISORDER OF John Doe
  ** CONFUSED
CONFUSED not a recognized response
What is THE THOUGHT PATTERN OR THOUGHT DISORDER OF John Doe
Expected responses are: NORMAL PROLIXIC TANGENTIAL CONFABULATION ETC>
Enter HELP for list of user options.
```

[The initial response was incorrect, so the user was reminded of some of the correct responses. He then requests a display of the entire list. Note that both of these capabilities are part of the core of MYCIN itself. Applying it to this new domain required more than supplying the relevant list of acceptable answers.]

```
  ** ?
  Expected responses are:  NORMAL PROLIXIC TANGENTIAL CONFABULATION
  RETARDED LOOSE CONCRETE AUTISTIC DELUSIONAL WORD-SALAD MANICY MUTE
  Enter HELP for list of user options.
  ** TANGENTIAL
  9) Has any biological relative of John Doe been evaluated or treated
     for a mental or psychiatric problem
  ** N
  10) What is the single word which best describes John Doe's behavior
  **
  What is the best single word description of John Doe's behavior
  Expected responses are: NORMAL AVERAGE UNREMARKABLE CATATONIC-EXCITEMENT
  etc.
  Enter HELP for list of user options.
  ** HYPERACTIVE
  11) What is the single word which best describes John Doe's mood
  ** LABILE
  12) WHAT IS THE SINGLE WORD WHICH BEST DESCRIBES THE EMOTIONS OR FEELINGS
      OF John Doe
  ** ELATED
  13) Does John Doe tend to feel worse or be more symptomatic for the
      first several hours after awakening for the day
  ** WHY

[i.e. WHY is it important to determine whether or not PATIENT-1 tends
     to feel worse or be more symptomatic for the first several hours
     after awakening for the day}

[4.0] This will aid in determining the DIAGNOSIS OF PATIENT-1.
     If
        [4.1] John Doe tends to feel worse or be more symptomatic for
                the first several hours after awakening for the day
     then
        there is weakly suggestive evidence (.45) that THE DIAGNOSIS OF
           john doe is depression
     [RULE017]
```

[All the standard explanatory capabilities of the core system extend to the new domain without additional programming effort.]

```
  [back to question 13...]
  ** N
  14) Does John Doe have early morning insomnia
  ** N
  15) Please specify the number of pounds that John Doe lost or gained
      in the 2 months prior to seeking medical or psychiatric help.
      Estimate if necessary.  Precede weight LOSS with a MINUS sign (for
      example: -8 - a weight loss of (approximately) 8 pounds within the
      2 month period prior to seeking professional help)

  ** 5
  16) Has psychological testing been ordered on John Doe
  ** N
  17) ARE THE PERCEPTIONS OF John Doe NORMAL, i.e., NEITHER DISTORTED
      NOR DISORDERED
  ** N
  18) DOES John Doe HAVE DEPERSONALIZATION
  ** N
  19) DOES John Doe HAVE EXPERIENCES OF ALIENATION and/or EXPERIENCES OF
      INFLUENCE
  ** N
  20) DOES John Doe HAVE INCOMPLETE AUDITORY HALLUCINATIONS and/or OTHER
      HALLUCINATIONS
  ** Y
  21) DOES John Doe HAVE COMPLETE AUDITORY HALLUCINATIONS and/or THOUGHT
      BROADCASTING
  ** N
  22) what is John Doe's level of consciousness
  **
  What is THE LEVEL OF CONSCIOUSNESS OF John Doe
  Expected responses are:  HYPERALERT VIGILANT ALERT NORMAL etc.
  Enter HELP for list of user options.
  ** VIGILANT
  23) Is this the first episode of significant mental disturbance that
      john doe has had
  ** WHY

[i.e. WHY is it important to determine whether or not this is PATIENT-1's
     first episode of significant mental disturbance}

[8.0] This will aid in determining THE TREATMENT NAME OF PATIENT-1.
     If
        [8.1] THE DIAGNOSIS OF John Doe is mania, and
        [8.2] this is not John Doe's first episode of significant mental
                 disturbance
     then
        there is strongly suggestive evidence (.9) that THE TREATMENT
         NAME OF John Doe is lithium
     [RULE071]

  [back to question 23...]
     [The system has finished with the diagnostic phase, and asks a
     question to help determine the appropriate therapy.]
  ** Y
```

[And finally the system presents its diagnosis and therapy recommendations. The numbers are used to give relative weightings to the conclusions: negative numbers indicate that the evidence tends to rule out that possibility.]

The diagnosis for patient 1 is:

ORGANIC-BRAIN-SYNDROME	(.84)
DEPRESSION	(.37)
MANIA	(.35)
SCHIZOPHRENIA	(.2)
PERSONALITY-DISORDER	(-.4)
NEUROSIS	(-.4)

So the treatment should be

EVALUATION	(.84)
ANTIDEPRESSANT	(.3)
NEUROLEPTIC	(.28)

Recently work has been directed toward expanding the system and revising the representation of psychiatric diagnosis and treatment recommendation.

We have also begun development of a small system to score the Minnesota Multiphasic Personality Inventory (MMPI) psychological test using empirically well established rules easily coded into the MYCIN system.

D. Up to date list of publications.

1. No reports of this work have been published to date.

2. Heiser, J.F. Computer-Aided Diagnosis of Psychiatric Patients. Presented to the Research Meeting, School of Engineering, University of California, Irvine, 7 October 1976.

3. Brooks, R. E. and Heiser, J.F. An Application of Artificial Intelligence to Psychiatry. Presented to:

   (a) Indian Institute of Technology, Madris, India, 28 September 1976, and

   (b) Madris Christian College, Madris, India, 3 October 1976.

4. Heiser, J.F. and Brooks, R. E. Artificial Intelligence in Psychopharmacology. Accepted for presentation at the VI World Congress of Psychiatry, Honolulu, Hawaii, 28 August - 3 October 1976.

E. Funding Status

1. Current Funding

a. Personnel

i. The principal investigator, Jon F. Heiser, M.D., co-investigator Ruven E. Brooks, Ph.E., and Pharmacist, Pierre J. Menard, Pharm. D., are full time employees of the University of California, Irvine.

ii. Resident physicians are employees of the University of California Irvine and the Long Beach Veterans Administration Hospital and have worked on this project during elective periods of their psychiatric residency for which they received training credit.

iii. Medical students working on this project either participated for academic credit during elective periods or were supported by National Institute for Mental Health fellowships for medical student research.

iv. Two undergraduate students (Thomas E. Holthus, and Darryl Hansen) are also working on this project for academic credit during elective periods.)

v. Additional supporting staff such as secretaries are supplied by the University of California Irvine.

b. Office space, supplies and equipment including several data terminals with acoustic couplers, are supplied by the University of California Irvine.

c. No other sources of funds are currently being used.

2. Pending applications and renewals

a. A joint grant application (in collaboration with Dr. Bruce Buchanan, Stanford University) has been submitted to the Department of Health, Education, and Welfare; Public Health Service. The University of California, Irvine (Dr. Jon Heiser, Principal Investigator) part of the application requests a total budget of $147,655 over three years to begin July 1, 1977, with $46,423 requested for the first year.

b. An additional financial support for undergraduate student Thomas E. Holthus has been requested through funds allocated to University of California Irvine by the National Science Foundation (NSF) to assist in the development of new research workers.

II. Interactions with the SUMEX-AIM resource

A. Examples of collaboration and medical use of programs via SUMEX

1. As explained fully in the attached research grant application, the MYCIN group has been working informally with Dr. Heiser on the development of a knowledge base of decision criteria for psychopharmacology over the past two years.

B. Examples of sharing, contacts, and cross-fertilization with other SUMEX-AIM projects (via workshops, system facilities, personal contacts, etc.)

1. Dr. Heiser's introduction to the SUMEX-AIM project first occurred at the first AIM workshop held at Rutgers in June 1975.

2. Although Dr. Heiser had previously heard of the MYCIN project, his official collaboration with MYCIN resulted from discussions originating at the first AIM Workshop.

3. A collaborative experiment with Kenneth Mark Colby, M.D., and members of the PARRY project was developed, implemented and analyzed completely on SUMEX-AIM. Enclosed is a rough draft of a paper reporting this "Turing Test" which was performed on-line on SUMEX, with the psychiatrist-judges located at Irvine, the patient-person at UCLA and PARRY at SUMEX.

4. Much technical support has been received freely and continuously from the SUMEX staff and members of the MYCIN team, including basic instruction in the use of SUMEX, TENEX, and MYCIN, principles of knowledge representation in MYCIN, and on-going consultation for details of implementing HEADMED in MYCIN.

   Much information has been obtained during three visits to to SUMEX and MYCIN, but daily work in this project would be impossible without the ability to converse via links, messages, and telephone conversations with members of the SUMEX and MYCIN staffs.

C. Critique of User Services

It is difficult for naive users to acquire the necessary knowledge and skills to function effectively in SUMEX without making a site visit to SUMEX.

III. Follow on SUMEX grant period (8/78 - 7/83)

A. Long range user project goals and plans.

It will probably take at least five years to achieve the aims mentioned in "I.A." above. If limiting conditions in the application of MYCIN to the domain of clinical psychopharmacology are encountered, alternative systems for achieving the same goals may be developed. If progress is straight forward and completed in less than five years, attempts will be made to enrich the system with deeper models of the nature of psychiatric disorders and the action of psychopharmacological substances. Also, if the system works well using UCI psychiatrists and patients, consultation with a panel of national experts will be developed to increase the generality and power of the rule base.

B. Justification for continued use of SUMEX by your project.

We believe that this collaboration between the Stanford University MYCIN group, the University of Arizona infectious disease group, and the University of California at Irvine psychopharmacology group offers a unique opportunity to study the decision-making process in two domains: the chemotherapy of infectious diseases and the chemotherapy of psychiatric disorders. We believe that this methodological approach will markedly increase the potential range of applicability of our work.

C. Comments and Suggestions for Future Resource Goals, and Development Effort.

For those not geographically located at the SUMEX site, a stress on additional aid to users in the form of increasing the staff of user consultants, documentation writers, etc., would be preferable to an exclusive stress on additional hardware acquisition.

6.4.3 ORGAN CULTURE PROJECT

Application of Computer Science to Organ Culture

Professor Robert K. Lindsay and Dr. Maija Kibens
The University of Michigan, Ann Arbor

I) Summary of research program

The goal of this research project is to develop new methods for the design and analysis of organ culture experiments, using techniques of artificial intelligence.

The cultivation of organ fragments is an important method for the study of disease processes. In contrast to cell culture, organ culture is designed to inhibit outgrowth of cells and to deal with normal tissue relationships as they exist in the body, divorced from the complexities or organ interaction. The technique involves the maintenance of differentiated cells as a group within their normally associated tissues. With an ability to maintain differentiated tissues in culture, a direct histologic and biochemical assessment of factors influencing an organ is possible. Such a biologic model would permit investigation of the structural and functional effects of various substances directly on the target organ. With a chemically defined medium, the technique would allow a simultaneous evaluation of metabolites or hormones released by the organ fragments.

The research is being done in collaboration with Professors Raymond Kahn, Theodore Fischer, and William Burkel of the Department of Anatomy, the University of Michigan Medical School.

We have been working on methods of image analysis of microscope slides. This has been approached from two directions. On the one hand we are writing programs for special image analysis hardware. These programs will calculate various indices of the condition of the cultivated organ fragments based upon measured morphological features. The second approach is to translate the biologist's verbal descriptions of microscope slides into computer data structures which encode conditions not detectable by our image analysis programs, though readily seen and reported by trained human observers. We have developed a dictionary of anatomical terms and programs for morphological analysis. At present we are working on the syntactic analysis of the scientist's verbal descriptions.

A grant application titled "Application of Computer Science to Organ Culture" has been written and will be submitted to the National Institutes of Health on June 1, 1977. Current support is from the University of Michigan with computer services supplied by SUMEX-AIM.

II) Interactions with the SUMEX-AIM resource

We have had valuable contacts with members of the DENDRAL project and the MOLGEN project, which share certain goals and methods with our own work.

The resource services received from SUMEX-AIM continue to be excellent. The staff is very helpful, and the system is well-maintained and reliable. The only serious difficulties which arise are due to system saturation and limited file space.

III) Follow-on SUMEX grant period

Our proposal, if funded, would commit us to expanding our efforts to develop a histology knowledge base and methods to rationalize the design of organ culture experiments. This would involve heavier use by a larger group of the SUMEX-AIM resource. Our work to date, though of limited scope, is encouraging. The work is dependent upon continued availability of the SUMEX-AIM system, which we would like to see expanded not only to provide more services for present projects, but to include a wider range of relevant bio-medical and artificial intelligence research. The commonality of resource and the opportunities for communication which SUMEX-AIM provides are extremely valuable in our view. Given the community of resource consumers attracted by SUMEX-AIM, we think it would be an excellent focus for the encouragement of new techniques, new ideas in programming languages, and increased variety of input and output media.

6.4.4 NEUROPROSTHESES PROJECT

Neuroprostheses Project

M. G. Mladejovsky, Ph.D., Director
Division of Artificial Organs
University of Utah Medical Center
Salt Lake City, Utah 84112

I. Research Summary

Our research involves the investigation of artificial vision by electrical stimulation of visual cortex and artificial hearing by electrical stimulation of the cochlea. This effort has involved the collaboration of several people from many disciplines, not only from the University of Utah, but also from the Ear Research Institute, Los Angeles; University of Western Ontario, London, Ontario; and Columbia University, New York.

The instrumentation involved is controlled by a minicomputer system consisting of a PDP-8 and a PDP-11/05. Experimental protocols are implemented by programs running in the PDP-11. We sought access to SUMEX in order to use the BLISS-11 compiler which runs on the PDP-10. We are using BLISS-11 as the implementation language for an interactive programming system which will enable more flexible control and variation of our experiments.

The base language we are using is BALM (Malcolm Harrison, "BALM Programmer's Manual", Courant Institute, NYU, 1974). This language is defined in terms of an abstract machine called the MBALM machine. The plan of attack is as follows:

1) implement the MBALM machine in BLISS-11
2) bring up BALM, using a dummy garbage collector and no virtual memory
3) implement garbage collection and virtual memory
4) add floating point operations
5) add a graphics package
6) add real-time capabilities
7) provide an interface to PDP-11 machine language

The project has progressed to the point that step 2 is almost complete. This has involved installing a new version of BLISS-11 at SUMEX, writing software to allow file transfers between SUMEX and our PDP-11 (which is connected to the Utah-TIP as a terminal), writing MBALM and various support routines in BLISS-11, implementing an I/O package for BALM in assembly language, and performing a bootstrapping process with the BALM self-definition. Our schedule calls for completing steps 3, 4, and 5 by 1 July 1977. Steps 6 and 7 have not been planned in detail at this time.

We are planning to run the resulting programming system on our PDP-11/05 with 28K core, GT-40 graphics system, and running the RT-11 operating system. Modifying the system to run under a different operating system should be straightforward. However, whether the system will run efficiently on a machine with less than 20K core is questionable. It is too early now to say.

There have been no new publications by our group since our application was filed last year. Currently several papers are in progress but have not yet been submitted for publication. A partial list of previous publications is attached.

When the BALM system has reached a stable state, we will be happy to provide documentation and sources for it to anyone who requests them.

The support for our human experiments is provided by a grant from the Max C. Fleischmann Foundation. This grant expires 30 June 1977, and a renewal proposal is now being prepared.

II. Interactions with SUMEX

We have been perfectly satisfied with our use of SUMEX. By far our greatest use of the system has been of text editors and the BLISS-11 compiler.

We have also become acquainted through SUMEX with the OMNIGRAPH graphics package available from NIH and have obtained a copy of the OMNIGRAPH manual. We have not used OMNIGRAPH yet but may wish to in the future. We are considering the features of OMNIGRAPH in the design of the graphics package for our interactive system.

We are quite interested in using the MAINSAIL system being developed at SUMEX and have been told that RT-11 is one of the first operating systems under which it will be available.

III. Long-range Plans

Our plans for the period beyond July 1978 will depend to a large extent on results of experiments which have not yet been performed. Our use of SUMEX for the purpose of developing an interactive programming system will presumably be complete sometime in 1977. It is possible that future needs will require non-real-time access to a machine of greater capabilities than our PDP-11/05 and PDP-8.

IV. Publications

Dobelle, W. H., Mladejovsky, M. G., and Girvin, J.P. Artificial vision for the blind: electrical stimulation of visual cortex offers hope for a functional prosthesis. Science, 183, 1 February 1974, 440-444.

Dobelle, W. H., and Mladejovsky, M. G. Phosphenes produced by electrical stimulation of human occipital cortex and their application to the development of a prosthesis for the blind. J. Phsiol., 243, 1974, 553-576.

Dobelle, W. H., Mladejovsky, M. G., Evans, J. R., Roberts, T. S., and Girvin, J. P. 'Braille' reading by a blind volunteer by visual cortex stimulation. Nature, 259, 15 January 1976, 111-112.

Mladejovsky, M. G., Eddington, D. K., Evans, J. R., and Dobelle, W. H. A computer-based brain stimulation system to investigate sensory prostheses for the blind and deaf. IEEE Trans. Biomed. Eng., BME-23, 4 July 1976, 286-296.

Mladejovsky, M. G., Eddington, D. K., Dobelle, W. H., and Brackmann, D. E. Artificial hearing for the deaf by cochlear stimulation: pitch modulation and some parametric thresholds. Transactions of ASAIO, 21, 1975, 1-6.

6.4.5 MATHEMATICAL MODELING OF PHYSIOLOGICAL SYSTEMS

Mathematical Modeling of Physiological Systems

John J. Osborn, M.D., Director
Research Data Facility
The Institutes of Medical Sciences
San Francisco, California 94115

The overall goal of the Institutes of Medical Sciences's collaboration with SUMEX is the application of computer technology to clinical medicine. Our efforts during the past year have been in the fields of knowledge based engineering and mathematical modeling.

We are using our available computer based physiological measurement systems to provide the basis on which physiological interpretation is being developed using knowledge engineering, and to provide the data with which mathematical models are being developed using the SUMEX modeling facility.

Project support:

Granting Agency: NIH
Grant Number: MB00134
Total period of the award: 3 years
Current year: 3
Current funding: $46,570

Granting agency: NIH
Grant Number: HR42917
Total period of the award: 3 years
Current year: 3
Current funding: $198,839

BIOMEDICAL KNOWLEDGE ENGINEERING IN CLINICAL MEDICINE (KEMED)

The KEMED system is conceived as an application of the discipline of heuristic based programming to the interpretation of measurements made in clinical medicine. The long range goal of the project is to do research on a biomedical knowledge-based system for interpreting the clincal significance of physiological data. This interpretation will be used to aid in diagnostic decision making and the selection of therapeutic action. Even the best measurements often go unused because of the reasonable reluctance of clinical staff to make measurements whose results they only poorly understand and whose relation to clinical management is ambiguous. We will use techniques of biomedical knowledge engineering to extract and systematize the heuristic knowledge used by experts in the practice of their clinical art. These techniques will be used to construct and utilize a knowledge base to guide inference making by computer programs.

The first program in the KEMED system is designed for interpretation of standard pulmonary function laboratory test data. A knowledge base was developed for interpreting the relationship between measured flows, lung volumes, pulmonary diffusion capacity and pulmonary mechanics and the standard diagnoses of pulmonary function. The knowledge base includes interpretation of measured test results and diagnosis of the type and severity of any pulmonary disease which may be present. The program is being developed as an extension to the MYCIN formalism, and it makes extensive use of the MYCIN structures and programming system. Funding has been requested to continue this work.

MATHEMATICAL MODELING OF PHYSIOLOGICAL SYSTEMS

Mathematical models of the cardio-pulmonary system are being developed to extract clinical physiological information from data acquired by the patient monitoring system. two approaches are being taken: 1) parsimonious models of the dynamic behavior of CO_2 following an increase in inspired oxygen concentration are being developed for automated patient monitoring application, and 2) a detailed model of the regional behavior of radioactive tracers in the lung is being used as a standard for evaluation of the previous models. The MLAB (Modelling Laboratory) program, available on SUMEX is being used extensively for model development by simulating hypothesized models and for data analysis, i.e., identification of model parameters from experimental data. The CO_2 dilution method has been applied successfully in the ICU and additional funding requested. Two new methods for measuring regional lung function with radioactive tracers have been developed where MLAB was essential and further funding has been requested. MLAB was used to perform an error analysis of the method for measuring regional pulmonary shunt fraction. Also, using MLAB model simulation to understand the complex dynamics of 133-Xenon in the lung-tissue system, a method for measuring intraregional ventilation/perfusion ratio maldistribution has been developed which significantly extends the sensitivity of previous methods. A model of the oculatory system is presently being developed on MLAB in collaboration with the Smith-Kettlewell Institute of the Visual Sciences. We anticipate that their model will be used in the future for treatment of patients with strabismus.

Interface with SUMEX

We use SUMEX through the Tymshare network using a terminal. The text editing facilities of SUMEX, including both text editing and message sending, are excellent additions to our in-house facilities (PDP-11 based system). The message system is particularily useful for communicating ideas and questions with other colleagues using the SUMEX system. Our principal difficulty with SUMEX is turn-around time. Both the MYCIN amd MLAB systems are interactive, and the 30-60 second time response times associated with MYCIN and MLAB jobs are at best discouraging.

We have a strong desire to develop in-house capabilities in artificial intelligence. We have already invested significant numbers of hours in developing competence with the MYCIN system, and we are confident of developing an extremely capable staff in heuristic programming. An in-house AI computational capability is a more difficult capability to conceive. Developing artificial intelligence programming facility on a PDP-11 based system remains a significant long-term interest. The satellite capability offers both the potential of not continuing to provide additional load on SUMEX, and it offers the potential of more rapid interaction with the user.

The SUMEX facility contributed to the following grant applications and articles:

Requested Funding:

1) Biomedical Knowledge Engineering in Clinical Medicine (NIH)
2) Pulmonary Function in Acute Illness (NIH)
3) Computer Laboratory for Clinical Support (NIH)
4) Improvement in Regional VA/Q Resolution (NIH, USAF, USN)

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6.4.6 PUFF/VM PROJECT

PUFF/VM - Pulmonary Function and Ventilator Management Project

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Note: The PUFF/VM project is the outgrowth of the efforts of Prof. Feigenbaum's group at Stanford to establish new applications areas for AI in medical research. It represents a collaboration with Dr. Osborn's group which has been working on another AIM pilot project titled "Mathematical Modeling of Physiological Systems". A PUFF/VM proposal is currently pending with NIH and and PUFF/VM is being reviewed in parallel by the AIM Executive Committee for separate pilot status.

1. General Problem

Measurements of patient physiology have become universally accepted as important parts of the delivery of clinical medicine. Good, useful measurements often go unused, however, because of the legitimate resistance of attending staff to using measurements which they poorly understand. Thus, technology contributes to clinical medicine if:

-- It's so useful, economical and easy to use that everyone can use it (e.g.: SMA-12, Brain scanner, Paps)

-- It's so useful, economical and has been around long enough that many people have been trained to use it (e.g.: ECG in ICU).

The dissemination of new technology in clinical medicine is limited by the ability of the system of medical care delivery to accept and assimilate the interpretation of the results of the technology. Given that the technology is useful in knowledgeable hands, this rate of assimilation is related somewhat to cost, but more to the rate at which education progresses. The new computer axial tomography systems have been accepted rapidly (two neighboring hospitals near San Francisco made headlines when each tried to purchase $200,000 devices) because the measurements they make are useful, and they are readily interpreted by staff. A system of medical technology should:

-- Make clinically important physiological measurements;

-- Get data automatically, accurately [done often];

-- Recognize irrelevant data, poor data and artifact [rarely done];

-- Interpret clinical significance of data in light of limitations of the data collection and analysis [almost never done];

-- Operate economically.

Systematic interpretation of test data is both possible (if the problem has a restricted domain) and desirable (because interpretation will be consistent for all and usable without direct supervision of a specialist).

2. Objectives

2.1. Overall Objectives:

Our immediate objective is to develop a computer programming system for interpreting the clinical significance of measures of pulmonary function. We hope to develop this system for diagnostic use in the pulmonary function laboratory and to aid diagnosis and ventilator management of respiratory insufficiency in the intensive care unit. We hope to demonstrate the clinical effectiveness of such a system for improving the accuracy and timeliness of diagnosis.

Our long range goal is to develop an integrated system for making and interpreting measures of pulmonary function. We believe that this is possible because of the present and potential contribution of instrumentation and data analysis systems to the diagnosis and clinical management of pulmonary distress. We believe, in addition, that the discipline of knowledge-based heuristic programming is potentially the best basis on which to develop a system for automaticaly interpreting the results of the measures of pulmonary function.

We aim, in the long run, to develop an inexpensive enough implementation that the system will find wide acceptability in the delivery of clinical care.

2.2. Pulmonary Laboratory:

Our objective for this project is to develop a heuristic program for interpreting the results of standard pulmonary function tests. The program will identify the need for repeated measurements because of poor patient effort; identify the need for additional information in order to make a more definitive diagnosis; report and explain the reasons for primary and secondary diagnoses and severity of any disease state; identify the relation between diagnosis and any referral diagnosis; interpret any change from previous tests or limitations on the interpretation because of the test methodology and the patient effort. We propose to: implement the system using a significant extension of an existing system of heuristic methods; extend the existing system to add new pulmonary disease diagnosis decision rules; develop models for directing program execution, achieving faster performance, and detecting and interpreting the clinical situation in terms of any inconsistent data; facilitate model acquisition.

2.3. Intensive Care Unit (ICU):

Our objective for this project is to develop computer programs for a system to interpret results of tests of pulmonary function in the hospital Intensive Care Unit. The program will interpret and explain the results of test measurements used to diagnose respiratory insufficiency; suggest initial settings for a ventilator for the patient with respiratory insufficiency; diagnose need for change in ventilation for the patient on a mechanical ventilator; and diagnose appropriateness of moving forward or back in the process of weaning the patient from the ventilator. We will implement the system using a new heuristic based interpretation system capable of interpreting continuous data from the changing patient situation. The system will allow goal-oriented and data-driven invocation of interpretation rules from the knowledge base.

2.4. Progress Evaluation:

Our objective for this project is to conduct major evaluations of the direction and schedule of the above projects. These evaluations will be conducted near the end of the first and second years of the project. The evaluations will help assure the soundness of the computer science and the clinical investigations. Outside experts in clinical medicine and computer science will participate in the evaluation process.

2.5. Advantages of Collaborative Effort between IMS and the Stanford Heuristic Programming Project

The collaboration offers a complementary blend of medical and computer science knowledge:

-- Clinically important problems: Interpretation of pulmonary measurements, both in lab and ICU.

-- Auto data collection and analysis in pulmonary lab and in ICU using computer. Data has demonstrated value in clinical medicine; Well understood procedures for collection, interpretation, use of data.

-- Having computer data collection, automated interpretation is logical next step.

-- Use all power computer science has available; discard excess in application specific implementation after designing into implementation the important features.

-- The SUMEX charter from NIH includes exporting artificial intelligence techniques (AI) to a larger community, and IMS is an excellent potential colleague. IMS has real clinical problems which can use AI effectively; biomedical engineering, statistics, and mathematical formulation of problems to contribute to AI; strong clinical orientation to give AI practical use.

3. Specific Aims

A. Develop an integrated knowledge-based system for interpreting standard pulmonary function test results.

B. Develop an integrated knowledge-based system for interpreting tests and observations used for diagnosis and treatment of respiratory insufficiency in the ICU.

C. Conduct major project evaluations, using outside experts in clinical medicine and computer science, to review progress to date and to help identify promising directions for continuing research.

To these ends, we will:

1. Develop a knowledge base for pulmonary function laboratory test interpretation, including rules to:

   -- Interpret results from spirometry , body plethosmography and measurement of diffusion capacity for CO;

   -- Diagnose the presence and severity of obstruction, restriction and diffusion defects;

   -- Diagnose the presence and severity of obstructive subtypes (asthma, bronchitis, emphysema); and

   -- Identify poor test results and the need for new information to make a more definitive diagnosis.

2. Implement rules for pulmonary function test interpretation using a significant extension of the existing MYCIN formalism. Heuristic and mathematical models of "prototype" disease states will be used to:

   -- Identify the presence of supporting and conflicting evidence for a primary interpretation;

   -- Interpret the clinical significance of measured data both in terms of measured data , the patient history, and expected values for the typical case;

   -- Recognize and interpret the significance of inconsistent data; and -- Direct the invocation of rules, thereby speeding program operation.

3. Develop a knowledge base for interpreting tests and observations relevant to diagnosis and ventilator management of respiratory insufficiency:

   -- Interpret results of measurements of vital capacity, blood gases, respiratory pressures, volumes, gas concentrations; hemodynamics;

   -- Recommend procedure for setting up a ventilator for a patient;